REMARKS

Claims 1, 18, 20, 23, 24, 27, and 31-35 are pending in the application and stand rejected. Claims 1, 18, 27, and 34 have been amended. Claims 31 and 33 have been canceled. Reconsideration and allowance of Claims 1, 18, 20, 23, 24, 27, 32, 34, and 35 in view of the above amendments and following remarks is respectfully requested.

Entry of the Amendment

Applicants believe that the amendments to the specification and claims place the application in condition for allowance, do not raise issues of new matter, and do not require further consideration and/or search by the Examiner. Entry of the amendment is respectfully requested.

Claims 1, 18, 27, and 34 have been amended to recite that the polypeptide has the amino acid sequence corresponding to the 34 kDa C terminal portion of SEQ ID NO:2. Support for the amendments can be found throughout the specification as originally filed. See, for example, page 64, line 29 - page 65, line 14, and Example 3, starting at page 67, line 17.

The Cross-Reference to Related Applications section has been amended to comply with 37 CFR 1.121(b)(1)(ii). Specifically, deletions that are five characters or less are marked in double brackets and the inserted text regarding the correct filing date and reference to the Australian Application are marked by underlining.

A replacement abstract is submitted as a separate sheet in compliance with 37 CFR 1.72(b) to correct the spelling of "nucleotide".

The Objection to Claims 31 and 32

Claims 31 and 32 have been objected to under 37 C.F.R. 1.75(c), as being of improper dependent form. Claim 31 has been canceled. Claim 18, from which Claim 32 depends, has

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been amended. Applicants believe the amendment to Claim 18 overcomes the objection to Claim 32. Withdrawal of the objection is respectfully requested.

The Objection to the Amendment Filed May 21, 2008 Under 35 U.S.C. § 132(a)

The amendment filed May 21, 2008, has been objected to under 35 U.S.C. § 132(a) for introducing new matter into the disclosure. The Office Action states that the amendment to the sequence listing filed May 21, 2008, deleting the Glx (representing glutamine or glutamic acid) residue from the C-terminus of SEQ ID NO:2, and the amendment to the paragraphs at pages 13, 14, 58, and 59 of the specification, making corresponding changes to the length of polypeptide of SEQ ID NO:2 and to the length of the coding sequence for the polypeptide of SEQ ID NO:2, are new matter.

Applicants respectfully submit that the amendments filed May 21, 2008, correct an obvious error and do not introduce new matter because one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction. See MPEP 2163.07(II), first paragraph. Ever since the universal genetic code was deciphered in the early 1960's, it has been a basic tenet underlying modern molecular biological research. In particular, it is well established which codons, or grouping of three consecutive RNA nucleotides, specify each amino acid. It is well known that the RNA codons UAA, UAG, or UGA ("stop codons"), which read in the encoding DNA as TAA, TAG, or TGA, respectively, do not specify any amino acid, but rather signal the stop of the translation process. See Alberts, B., et al., "Molecular Biology of the Cell," 4th ed., Garland Science, Taylor & Francis Group, London, February 2002, Chap. 6, "How Cells Read the Genome: From DNA to Protein," pp. 336, 349-350 (attached hereto as **Exhibit A**). Applicants stated in their original application that the full length coding sequence of Bpmp-72 was found to be 1,692 nucleotides long and SEQ ID NO:2 designated Glx as the final, 564th amino acid. See, Application, page 13, lines

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7-9, and sequence listing page 4; see also Published Application, US 2007/0026017A, page 4, paragraph [0051] and page 28. However, both Figure 3 and the DNA SEQ ID NO:1 clearly show the TAA codon at the site corresponding to the described Glx. Any person skilled in the art would recognize TAA as a stop codon and that the amino acid sequence terminates after the Gln (glutamine) encoded by the immediately previous codon, CAG. Thus, any person skilled in the art would recognize that the inclusion of Glx in the protein sequence at the 564th position was a typographical error. Moreover, applicants submit that one skilled in the art would recognize the deletion of the Glx residue from the C-terminus of the sequence, and the deletion of the corresponding descriptive language in the specification, as the appropriate correction to the error because the change does not introduce frame shifts or in any way alter the relative relationships of the remaining amino acid residues to each other. As such, applicants respectfully submit that the amendment as filed on May 21, 2008, does not introduce new subject matter. Entry of that amendment and withdrawal of the objection is respectfully requested.

The Rejection of Claims 1, 18, 20, 23, 24, 27, and 32 Under 35 U.S.C. § 112, First Paragraph

Claims 1, 18, 20, 23, 24, 27, and 32 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Withdrawal of the rejection is requested for the following reasons.

The Office Action states that the amendment to the sequence listing filed May 21, 2008, introduces a polypeptide having 563 amino acids and not comprising a C-terminal Glx residue and that there is no original disclosure supporting such a polypeptide. For the reasons set forth above (The Objection to the Amendment Filed May 21, 2008), applicants submit that the amendments to the sequence and specification do not introduce new matter because one skilled in the art would recognize the existence of the error and the appropriate correction of the error. Withdrawal of the rejection is respectfully requested.

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The Rejection of Claims 31, 33, and 34 Under 35 U.S.C. § 112, First Paragraph

Claims 31, 33, and 34 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Withdrawal of the rejection is requested for the following reasons.

The Office Action states that there is no original disclosure supporting the recitation of a polypeptide comprising an amino acid sequence corresponding to amino acid residues 305 to 563 of SEQ ID NO:2, as occurs in the rejected claims.

Claims 31 and 33 have been canceled. Claim 34 has been amended to delete the recitation amino acid residues 305 to 563. In view of the cancellation of Claims 31 and 33 and the amendment of Claim 34, withdrawal of the rejection is respectfully requested.

The Rejection of Claims 1, 24, and 27 Under 35 U.S.C. § 112, First Paragraph

Claims 1, 24, and 27 have been rejected under 35 U.S.C. § 112, first paragraph, for failing to meet the enablement requirement. Withdrawal of the rejection is requested for the following reasons.

The Office Action states that the specification, while enabling for an isolated polypeptide comprising SEQ ID NO:2, the isolated polypeptide corresponding to the 34 kDa C-terminal portion thereof disclosed in Example 3, methods of treating a disease associated with *Brachyspira* species using the same, and compositions comprising the same, does not reasonably provide enablement for polypeptides comprising fragments of SEQ ID NO:2, e.g., comprising SEQ ID NOS:3-22, for peptides that are at least 90% homologous to SEQ ID NO:2, or its fragments, or for methods of using the same.

Claims 1, 24, and 27 have been amended to recite that the amino acid sequence corresponds to the 34 kDa C-terminal portion of SEQ ID NO:2. In view of the amendment to the rejected claims, withdrawal of the rejection is respectfully requested.

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The Rejection of Claims 1, 18, 20, 24, 27, and 31-35 Under 35 U.S.C. § 102(b)

Claims 1, 18, 20, 24, 27, and 31-35 have been rejected under 35 U.S.C. § 102(b) as being anticipated by the Tenaya et al. article (*Journal of Medical Microbiology 47*: 317-324) in view of applicants' admission of the prior art at page 1, lines 20-21, of the specification. Withdrawal of the rejection is requested for the following reasons.

Without acquiescing to the Examiner's position that the Tenaya reference inherently anticipates SEQ ID NO:2, and based on the Examiner's indication that the specification is enabled for a portion of the sequence, to advance prosecution, Claims 1, 18, 27, and 34 have been amended to recite "an amino acid sequence corresponding to the 34 kDa C terminal portion of SEQ ID NO:2." Applicants have established the ability of this specific portion of the polypeptide to protect against colonization by *B. piloscoli* after injection into chickens. See Application, page 71, line 23 - page 74, line 7. Tenaya does not disclose, teach, or suggest fragment of a protein corresponding to the 34 kDa C terminal portion of SEQ ID NO:2, as now recited in the amended claims. As such, the disclosure of Tenaya cannot inherently anticipate this specific 34 kDa C-terminal portion of SEQ ID NO:2. Therefore, withdrawal of the rejection is respectfully requested.

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CONCLUSION

In view of the above amendments and foregoing remarks, applicants believe that Claims 1, 18, 20, 23, 24, 27, 32, 34, and 35 are in condition for allowance. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney at 206.695.1755.

Respectfully submitted,

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EXHIBIT A

MOLECULAR BIOLOGY OF THE CELL

fourth edition

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Alexander Johnson

Julian Lewis

Martin Raff

Keith Roberts

Peter Walter

Garland Science
Taylor & Francis Group

GCA GCC GCG GCU	AGA AGG CGA CGC CGG CGU	GAC GAU	AAC AAU	UGC UGU	GAA GAG	CAA CAG	GGA GGC GGG GGU	CAC CAU	AUA AUC AUU	UUA UUG CUA CUC CUG CUU	AAA AAG	AUG	UUC UUU	CCA CCC CCG CCU	AGC AGU UCA UCC UCG UCU	ACA ACC ACG ACU	UGG	UAC UAU	GUA GUC GUG GUU	UAA UAG UGA
Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	stop
A	R	D	N	C	E	Q	G	H	I	L	K	M	F	P	S	T	W	Y	V	

when it was posed as the "coding problem": how is the information in a linear sequence of nucleotides in RNA translated into the linear sequence of a chemically quite different set of subunits—the amino acids in proteins? This fascinating question stimulated great excitement among scientists at the time. Here was a cryptogram set up by nature that, after more than 3 billion years of evolution, could finally be solved by one of the products of evolution—human beings. And indeed, not only has the code been cracked step by step, but in the year 2000 the elaborate machinery by which cells read this code—the ribosome—was finally revealed in atomic detail.

An mRNA Sequence Is Decoded in Sets of Three Nucleotides

Once an mRNA has been produced, by transcription and processing the information present in its nucleotide sequence is used to synthesize a protein. Transcription is simple to understand as a means of information transfer: since DNA and RNA are chemically and structurally similar, the DNA can act as a direct template for the synthesis of RNA by complementary base-pairing. As the term *transcription* signifies, it is as if a message written out by hand is being converted, say, into a typewritten text. The language itself and the form of the message do not change, and the symbols used are closely related.

In contrast, the conversion of the information in RNA into protein represents a **translation** of the information into another language that uses quite different symbols. Moreover, since there are only four different nucleotides in mRNA and twenty different types of amino acids in a protein, this translation cannot be accounted for by a direct one-to-one correspondence between a nucleotide in RNA and an amino acid in protein. The nucleotide sequence of a gene, through the medium of mRNA, is translated into the amino acid sequence of a protein by rules that are known as the **genetic code**. This code was deciphered in the early 1960s.

The sequence of nucleotides in the mRNA molecule is read consecutively in groups of three. RNA is a linear polymer of four different nucleotides, so there are $4 \times 4 \times 4 = 64$ possible combinations of three nucleotides: the triplets AAA, AUA, AUG, and so on. However, only 20 different amino acids are commonly found in proteins. Either some nucleotide triplets are never used, or the code is redundant and some amino acids are specified by more than one triplet. The second possibility is, in fact, the correct one, as shown by the completely deciphered genetic code in Figure 6–50. Each group of three consecutive nucleotides in RNA is called a **codon**, and each codon specifies either one amino acid or a stop to the translation process.

This genetic code is used universally in all present-day organisms. Although a few slight differences in the code have been found, these are chiefly in the DNA of mitochondria. Mitochondria have their own transcription and protein synthesis systems that operate quite independently from those of the rest of the cell, and it is understandable that their small genomes have been able to accommodate minor changes to the code (discussed in Chapter 14).

In principle, an RNA sequence can be translated in any one of three different **reading frames**, depending on where the decoding process begins (Figure 6–51). However, only one of the three possible reading frames in an mRNA encodes the required protein. We see later how a special punctuation signal at the beginning of each RNA message sets the correct reading frame at the start of protein synthesis.

Figure 6–50 The genetic code. The standard one-letter abbreviation for each amino acid is presented below its three-letter abbreviation (see Panel 3–1, pp. 132–133, for the full name of each amino acid and its structure). By convention, codons are always written with the 5′-terminal nucleotide to the left. Note that most amino acids are represented by more than one codon, and that there are some regularities in the set of codons that specifies each amino acid. Codons for the same amino acid tend to contain the same nucleotides at the first and second positions, and vary at the third position. Three codons do not specify any amino acid but act as termination sites (stop codons), signaling the end of the protein-coding sequence. One codon—AUG—acts both as an initiation codon, signaling the start of a protein-coding message, and also as the codon that specifies methionine.

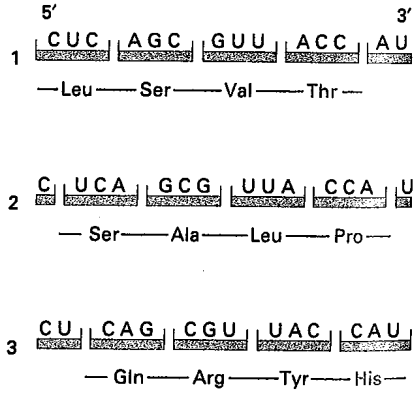
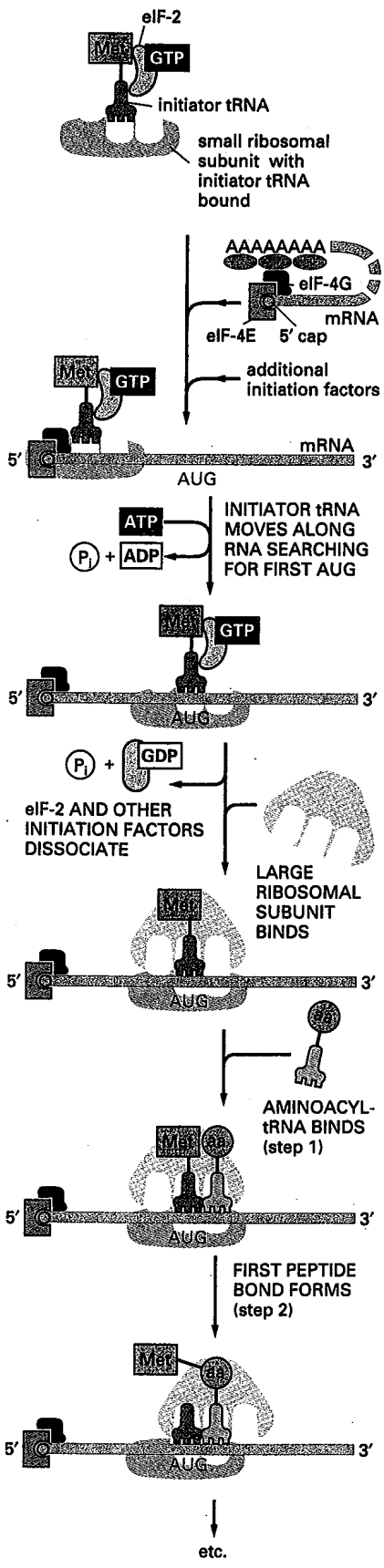


Figure 6–51 The three possible reading frames in protein synthesis. In the process of translating a nucleotide sequence *(blue)* into an amino acid sequence *(green)*, the sequence of nucleotides in an mRNA molecule is read from the 5′ to the 3′ end in sequential sets of three nucleotides. In principle, therefore, the same RNA sequence can specify three completely different amino acid sequences, depending on the reading frame. In reality, however, only one of these reading frames contains the actual message.

Figure 6–71 The initiation phase of protein synthesis in eucaryotes. Only three of the many translation initiation factors required for this process are shown. Efficient translation initiation also requires the poly-A tail of the mRNA bound by poly-A-binding proteins which, in turn, interact with eIF4G. In this way, the translation apparatus ascertains that both ends of the mRNA are intact before initiating (see Figure 6–40). Although only one GTP hydrolysis event is shown in the figure, a second is known to occur just before the large and small ribosomal subunits join.



methionine is usually removed later by a specific protease. The initiator tRNA has a nucleotide sequence distinct from that of the tRNA that normally carries methionine.

In eucaryotes, the initiator tRNA (which is coupled to methionine) is first loaded into the small ribosomal subunit along with additional proteins called **eucaryotic initiation factors**, or **eIFs** (Figure 6–71). Of all the aminoacyl tRNAs in the cell, only the methionine-charged initiator tRNA is capable of tightly binding the small ribosome subunit without the complete ribosome present. Next, the small ribosomal subunit binds to the 5′ end of an mRNA molecule, which is recognized by virtue of its 5′ cap and its two bound initiation factors, eIF4E (which directly binds the cap) and eIF4G (see Figure 6–40). The small ribosomal subunit then moves forward (5′ to 3′) along the mRNA, searching for the first AUG. This movement is facilitated by additional initiation factors that act as ATP-powered helicases, allowing the small subunit to scan through RNA secondary structure. In 90% of mRNAs, translation begins at the first AUG encountered by the small subunit. At this point, the initiation factors dissociate from the small ribosomal subunit to make way for the large ribosomal subunit to assemble with it and complete the ribosome. The initiator tRNA is now bound to the P site, leaving the A-site vacant. Protein synthesis is therefore ready to begin with the addition of the next aminoacyl tRNA molecule (see Figure 6–71).

The nucleotides immediately surrounding the start site in eucaryotic mRNAs influence the efficiency of AUG recognition during the above scanning process. If this recognition site is quite different from the consensus recognition sequence, scanning ribosomal subunits will sometimes ignore the first AUG codon in the mRNA and skip to the second or third AUG codon instead. Cells frequently use this phenomenon, known as "leaky scanning," to produce two or more proteins, differing in their N-termini, from the same mRNA molecule. It allows some genes to produce the same protein with and without a signal sequence attached at its N-terminus, for example, so that the protein is directed to two different compartments in the cell.

The mechanism for selecting a start codon in bacteria is different. Bacterial mRNAs have no 5′ caps to tell the ribosome where to begin searching for the start of translation. Instead, each bacterial mRNA contains a specific ribosome-binding site (called the Shine–Dalgarno sequence, named after its discoverers) that is located a few nucleotides upstream of the AUG at which translation is to begin. This nucleotide sequence, with the consensus 5′-AGGAGGU-3′, forms base pairs with the 16S rRNA of the small ribosomal subunit to position the initiating AUG codon in the ribosome. A set of translation initiation factors orchestrates this interaction, as well as the subsequent assembly of the large ribosomal subunit to complete the ribosome.

Unlike a eucaryotic ribosome, a bacterial ribosome can therefore readily assemble directly on a start codon that lies in the interior of an mRNA molecule, so long as a ribosome-binding site precedes it by several nucleotides. As a result, bacterial mRNAs are often *polycistronic*—that is, they encode several different proteins, each of which is translated from the same mRNA molecule (Figure 6–72). In contrast, a eucaryotic mRNA generally encodes only a single protein.

Stop Codons Mark the End of Translation

The end of the protein-coding message is signaled by the presence of one of three codons (UAA, UAG, or UGA) called *stop codons* (see Figure 6–50). These are not recognized by a tRNA and do not specify an amino acid, but instead signal

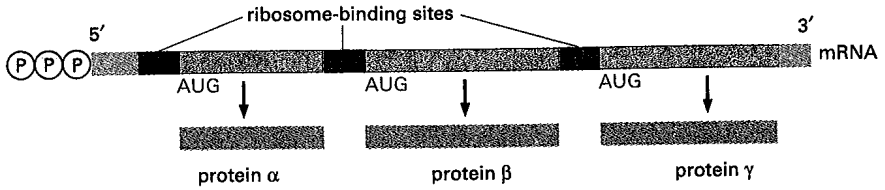


Figure 6–72 Structure of a typical bacterial mRNA molecule. Unlike eucaryotic ribosomes, which typically require a capped 5′ end, procaryotic ribosomes initiate transcription at ribosome-binding sites (Shine–Dalgarno sequences), which can be located anywhere along an mRNA molecule. This property of ribosomes permits bacteria to synthesize more than one type of protein from a single mRNA molecule.

to the ribosome to stop translation. Proteins known as *release factors* bind to any ribosome with a stop codon positioned in the A site, and this binding forces the peptidyl transferase in the ribosome to catalyze the addition of a water molecule instead of an amino acid to the peptidyl-tRNA (Figure 6–73). This reaction frees the carboxyl end of the growing polypeptide chain from its attachment to a tRNA molecule, and since only this attachment normally holds the growing polypeptide to the ribosome, the completed protein chain is immediately released into the cytoplasm. The ribosome then releases the mRNA and separates into the large and small subunits, which can assemble on another mRNA molecule to begin a new round of protein synthesis.

Release factors provide a dramatic example of *molecular mimicry*, whereby one type of macromolecule resembles the shape of a chemically unrelated molecule. In this case, the three-dimensional structure of release factors (made entirely of protein) bears an uncanny resemblance to the shape and charge distribution of a tRNA molecule (Figure 6–74). This shape and charge mimicry allows the release factor to enter the A-site on the ribosome and cause translation termination.

During translation, the nascent polypeptide moves through a large, water-filled tunnel (approximately 10 nm × 1.5 nm) in the large subunit of the ribosome (see Figure 6–68C). The walls of this tunnel, made primarily of 23S rRNA, are a patchwork of tiny hydrophobic surfaces embedded in a more extensive hydrophilic surface. This structure, because it is not complementary to any peptide structure, provides a "Teflon" coating through which a polypeptide chain can easily slide. The dimensions of the tunnel suggest that nascent proteins are largely unstructured as they pass through the ribosome, although some α-helical regions of the protein can form before leaving the ribosome tunnel. As it leaves the ribosome, a newly-synthesized protein must fold into its proper three-dimensional structure to be useful to the cell, and later in this chapter we discuss how this folding occurs. First, however, we review several additional aspects of the translation process itself.

Proteins Are Made on Polyribosomes

The synthesis of most protein molecules takes between 20 seconds and several minutes. But even during this very short period, multiple initiations usually take place on each mRNA molecule being translated. As soon as the preceding ribosome has translated enough of the nucleotide sequence to move out of the way, the 5′ end of the mRNA is threaded into a new ribosome. The mRNA molecules being translated are therefore usually found in the form of *polyribosomes* (also known as *polysomes*), large cytoplasmic assemblies made up of several ribosomes spaced as close as 80 nucleotides apart along a single mRNA molecule (Figure 6–75). These multiple initiations mean that many more protein

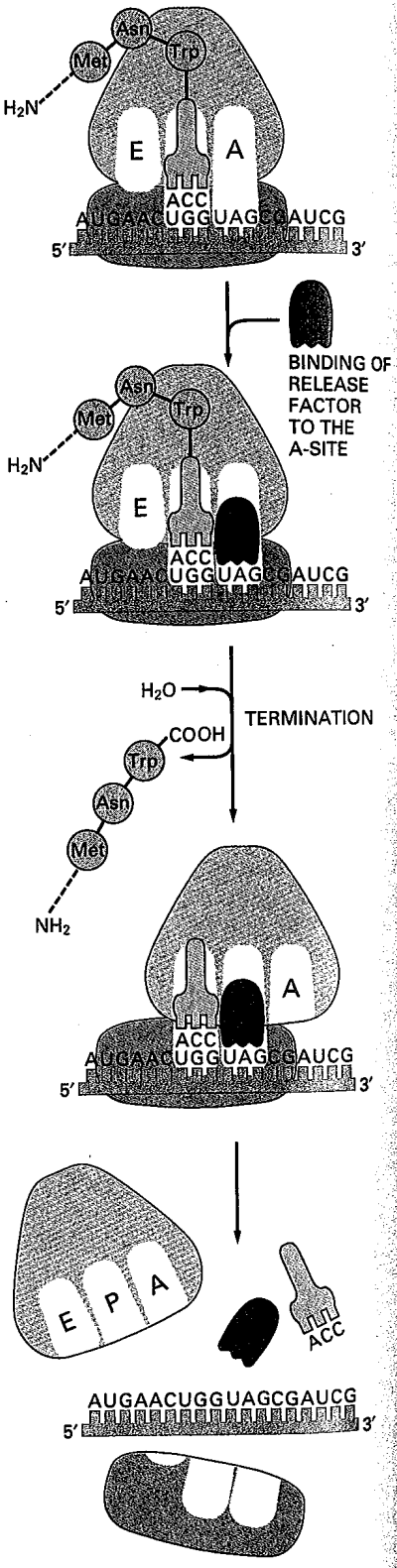


Figure 6–73 The final phase of protein synthesis. The binding of a release factor to an A-site bearing a stop codon terminates translation. The completed polypeptide is released and, after the action of a *ribosome recycling factor* (not shown), the ribosome dissociates into its two separate subunits.